MAIL STOP APPEAL BRIEF-PATENTS
Attorney Docket No. 27579U

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

ROSCHER et al. Confirmation No.: 3799

Serial No: 10/589,871 Group Art Unit: 1627

Appeal No. 2011-013132

Filed: August 18, 2006 Examiner: CHONG, Y.S.

For: **CICLESONIDE AND GLYCOPYRRONIUM COMBINATION**

REPLY BRIEF

This Reply Brief is filed in response to the Examiner's Answer mailed April 20, 2011 and the Decision on Petition mailed July 14, 2011. In the Decision on Petition, the Chief Administrative Patent Judge, James D. Smith, granted appellants two months from the date of the Decision to file a Reply Brief, or by September 14, 2011. Accordingly, this paper is timely filed.

1. **Status of Claims**

The status of the claims is as follows upon filing of this Reply Brief:

Claims cancelled: 2-3, 5-7 and 12-13

Claims withdrawn from consideration but not cancelled: 14-18

Claims pending: 1, 4, 8-11 and 14-19

Claims objected to: None

Claims allowed: None

Claims rejected: 1, 4, 8-11 and 19

The claims on appeal are 1, 4, 8-11 and 19.

2. Grounds of Rejection to be Reviewed on Appeal

A. Rejection of claims 1, 4, 8-11 and 19 under 35 USC § 103(a)

Whether the identified claims are unpatentable under 35 USC § 103(a) as obvious over Noe et al. (US Patent No. 6,613,795) in view of Postma et al. ("Treatment of asthma by the inhaled cortiocosteroid ciclesonide given either in the morning or evening", Eur. Respir. J. 2001; 17:1083-1088).

3. Argument

A. Rejection of claims 1, 4, 8-11 and 19 under 35 USC § 103(a)

In the Examiner's Answer, the Examiner has newly rejected claims 1, 4, 8-11 and 19 under 35 USC §103(a) as being unpatentable over Noe et al. in view of Postma et al. This rejection takes the place of the now withdrawn rejection of these claims under 35 USC §103(a) as being unpatentable over Noe et al. in view of Wurst et al. (US 2007/0025923) in view of appellants' successful arguments.

In the Examiner's Answer, the Examiner has attempted to establish a new *prima facie* case of obviousness over the presently pending claims by introducing the disclosure of Postma et al. and combining it with Noe et al. Appellants respectfully traverse this new rejection of the claims.

Appellants respectfully submit that this new combination of references does not establish a *prima facie* case of obviousness over the presently pending claims.

The relevant legal authority for establishing a *prima facie* case of obviousness is outlined in the Appeal Brief on pages 9-10 and will not be repeated here. However, appellants will respectfully remind the Board that "[a] reference must be considered for everything it teaches by way of technology and is not limited to the particular invention it is describing and attempting to protect. On the issue of obviousness, the combined teachings of the prior art as a whole must be considered." *See EWP Corp. v. Reliance Universal, Inc.*, 755 F.2d 898, 907 (Fed. Cir. 1985). Further, appellants respectfully note that "[i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly

suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241 (CCPA 1965); *see also Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448-49 (Fed. Cir. 1986). Finally, when evaluating the obviousness of a particular invention, the law requires considering the "whole" of the prior art. See *In re Keller*, 642 F.2d 413, 425 (CCPA 1981).

Therefore, it is well-settled law that the Examiner is not allowed to use hindsight reconstruction to pick and choose certain claimed elements from different references to arrive at applicants' or appellants' claimed subject matter. Further, the Examiner must consider the entire disclosure of the cited references to establish her *prima facie* case.

In the instant case, appellants respectfully note that the Examiner has made a simple and conclusory assertion based on hindsight that, because Noe et al. disclose (3R,2'R)-3-[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidinium and the carrier lactose, and because Postma et al. disclose ciclesonide, then the combination of these three very specific components would be obvious to the ordinary skilled artisan. However, the Examiner has failed to consider the entire teachings of Noe et al. and Postma et al. which would not lead a person of ordinary skill in the art to combine the teachings of these two references to arrive at the presently claimed subject matter.

In particular, the Examiner has seemingly ignored that Noe et al., at col. 9, lines 18-23, state the following:

> "Owing to the fact that [the enantiomeric compounds] can be administered at a particularly low dosage, because of their high affinity, and the fact that they have a particularly favorable subtype profile they afford the therapeutic results more efficiently, and have a considerably reduced potential for side effects."

Further, Noe et al. state at col. 9, lines 43-45:

> "To summarize, it can be stated that enantiomerically pure esters of formula I are distinguished from the prior art by their pharmacodynamics selectivity."

Further, Noe et al. state at col. 9, lines 54-67:

> "Compared with the nonselective parasympatholytics which have previously been used, they differ considerably in the pharmacological properties, owing to their defined subtype selectivity. Compared with the known mixtures of stereoisomers and racemates, the compounds can additionally be employed at a particularly low dosage, thus minimizing side effects.
>
> Accordingly, the invention prefers the use of enantiomerically pure esters (3R, 2'R....) of the formula I in medicaments for the therapy of spasms of the smooth muscles of the gastrointestinal tract and the urogenital tract and for the treatment of obstructive respiratory diseases (brochial asthma, chronic bronchitis)."

Thus, the enantiomeric compound (3R,2'R)-3-[(cyclopentylhydroxyphenylacetyl)-oxy]-1,1-dimethylpyrrolidinium disclosed by Noe et al. would be recognized by a person of ordinary skill as a compound that may be successfully administered alone at a very low dosage with minimal side effects.

Accordingly, due to the potential of (3R,2'R)-3-[(cyclopentylhydroxyphenylacetyl)-oxy]-1,1-dimethylpyrrolidinium to deliver promising results in the treatment of obstructive respiratory diseases at a very low dosage with minimal side effects when administered

alone as outlined in Noe et al., the ordinary skilled artisan armed with this knowledge would not likely have any motivation to combine this particular compound with any other compound to perhaps achieve better results or a more favorable dosing or side effect profile.

The disclosure of Postma et al. would not provide the ordinary skilled artisan with any such motivation. In particular, appellants note that Postma et al. expressly states on page 1083, col. 2 that "[c]iclesonide is currently developed for once-daily dosing in patients with mild-to-moderate asthma". This dosing regimen stands in contrast to other inhaled corticosteroids which have been recommended to be administered twice or even four times daily as shown on page 1083, col. 1. Postma et al. recognize that "compliance to inhaled steroids is often poor" and "[a]mong the manifold reasons underlying noncompliance, complicated regimens and dosing frequency are considered to be significant factors." See page 1083, col. 1.

With the likely preferred once-per-day dosing regimen, Postma et al. indicated that the specific steroid ciclesonide achieved a "very effective" rating in 71% of patients who took ciclesonide in the evening, an "effective" rating in 63% of patients who took ciclesonide in the morning or evening, and a "very effective" rating in 61% of patients who took ciclesonide in the morning. Less than 4% of patients in the Postma et al. study experienced lack of efficacy. See page 1086, col. 2.

Further, Postma et al. noted that "[t]he safety data of the current trial suggest that ciclesonide was well tolerated", which was "in line with the results of a study in healthy volunteers where the 24-h mesor for serum cortisol under ciclesonide (800µg), given

either in the morning or evening for one week, was 2-6% lower compared to placebo indicating that ciclesonide lacks relevant systemic effects." See page 1087, col. 2.

Accordingly, due to the potential of ciclesonide to deliver promising results in the treatment of asthma in a preferred once-per-day dosing with a low risk for systemic effects when administered alone as outlined in Postma et al., the ordinary skilled artisan armed with this knowledge would not likely have any motivation to combine ciclesonide with any other compound to perhaps achieve better results or a more favorable dosing or side effect profile.

As such, the Examiner has failed to consider the full scope of the Noe et al. and Postma et al. references "necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau,* Id. Accordingly, the ordinary skilled artisan would have no motivation to combine the (3R,2'R)-3-[(cyclopentylhydroxyphenylacetyl)-oxy]-1,1-dimethylpyrrolidinium and lactose components of Noe et al. with the ciclesonide component of Postma et al. to arrive at the presently claimed subject matter. As such, no *prima facie* case of obviousness exists.

In view of the foregoing, appellants respectfully request that the Board reverse the Examiner's rejection and remand this case to the Examiner for the immediate allowance of the pending claims. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account No. 14-0112.

Respectfully submitted,

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Date: September 14, 2011

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